10676089

=> d his

(FILE 'HOME' ENTERED AT 14:50:52 ON 02 JUL 2005)

FILE 'MEDLINE' ENTERED AT 14:51:00 ON 02 JUL 2005

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L1            78 S RAR ANTAGONIST?
L2          2641 S RAR
L3          4870 S ATOPY
L4         21707 S PSORIASIS
L5            12 S L2 (P) L4
L6             0 S L2 (P) L3
L7             0 S L2 AND L3
L8          7800 S RETINOID
L9             3 S L8 AND ATOPY
L10            7 S CUTANEOUS ATOPY
L11           50 S RESPIRATORY ATOPY
L12            0 S GINGIVAL HYPERTROPY
L13          361 S GINGIVAL HYPERTROPHY
L14            0 S L11 AND L13
L15            0 S L13 AND L2
L16            1 S L13 AND L4
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L9 ANSWER 1 OF 3 MEDLINE on STN
AN 2001455618 MEDLINE
DN PubMed ID: 11502488
TI Could bronchial asthma be an endogenous, pulmonary expression of **retinoid** intoxication?.
AU Mawson A R
CS College of Health Sciences, Des Moines University-Osteopathic Medical Center, 3200 Grand Avenue, Des Moines, Iowa 50312, USA.. anthony.mawson@dmu.edu
SO Frontiers in bioscience : a journal and virtual library, (2001 Aug 1) 6 D973-85. Electronic Publication: 2001-08-01. Ref: 124
Journal code: 9709506. ISSN: 1093-4715.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20010815
Last Updated on STN: 20020122
Entered Medline: 20011213

L9 ANSWER 2 OF 3 MEDLINE on STN
AN 89340009 MEDLINE
DN PubMed ID: 2527214
TI [Successful **retinoid** therapy of Netherton syndrome]. Erfolgreiche Retinoidtherapie des Netherton-Syndroms.
AU Hartschuh W; Hausser I; Petzoldt D
CS Hautklinik, Ruprecht-Karls-Universitat Heidelberg.
SO Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und verwandte Gebiete, (1989 Jul) 40 (7) 430-3.
Journal code: 0372755. ISSN: 0017-8470.
CY GERMANY, WEST: Germany, Federal Republic of
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 198909
ED Entered STN: 19900309
Last Updated on STN: 20020125
Entered Medline: 19890919

L9 ANSWER 3 OF 3 MEDLINE on STN
AN 84192681 MEDLINE
DN PubMed ID: 6718040
TI [The Netherton syndrome: clinical characteristics, differential diagnosis and new ways of therapy]. Das Netherton-Syndrom: Klinische Charakteristik, differential-diagnostische Abgrenzung und neue Wege der Therapie.
AU Haas O A; Martins da Cunha A; Gadner H; Stingl G; Kornmuller R
SO Padiatrie und Padologie, (1984) 19 (2) 153-9.
Journal code: 0022370. ISSN: 0030-9338.
CY Austria
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals

10676089

EM 198406
ED Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840613

=> d 1-3 kwic

L9 ANSWER 1 OF 3 MEDLINE on STN
TI Could bronchial asthma be an endogenous, pulmonary expression of **retinoid** intoxication?.
AB . . . 17 million people in the United States, including 4.8 million children. A striking increase in asthma and other forms of **atopy** has occurred in children in the U.S. and other western countries during the past 30 years. Several studies have reported an inverse association between childhood infectious illness and the development of **atopy** , suggesting that certain forms of infection protect against and even inhibit asthma. This may involve a shift in the balance. . . childhood infection, retinoids (vitamin A and its congeners) accumulate in the lung. Later, upon exposure to known triggers for asthma, **retinoid** metabolites may be produced in such high concentration that they produce an acute, localized form of **retinoid** intoxication, recognized as status asthmaticus.

L9 ANSWER 2 OF 3 MEDLINE on STN
TI [Successful **retinoid** therapy of Netherton syndrome]. Erfolgreiche Retinoidtherapie des Netherton-Syndroms.
AB A young patient with Netherton's syndrome characterized by the classic triad of ichthyosis linearis circumflexa, trichorhexis invaginata and **atopy** was treated with Acitretin, a new **retinoid** preparation: 35 mg Acitretin/day resulted in a severe, erosive dermatitis which necessitated interruption of therapy. Even with 10 mg/day the. . . Acitretin drastically reduced the deposition of intra- and extracellular material and normalized keratinization. Our results underline the importance of starting **retinoid** therapy in Netherton's syndrome at a low dosage and adjusting it carefully in each case with reference to the skin. . .

L9 ANSWER 3 OF 3 MEDLINE on STN
AB . . . trait. It is defined by a triad of symptoms: congenital ichthyosiform erythrodermia , trichorrhexis invaginata et nodosa ("bamboo hair") and **atopy.** Additional disorders affect the immune system, the metabolism of amino acids and the physical development. On the basis of a. . . the disease are more clearly defined. A new form of treatment--a combination of photochemotherapy (PUVA) and systematic application of aromatic **retinoid**--has so far proved to be successful. In order to establish an accurate diagnosis--a prerequisite for this promising therapeutic approach--diseases with. . .

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(FILE 'HOME' ENTERED AT 14:50:52 ON 02 JUL 2005)

FILE 'MEDLINE' ENTERED AT 14:51:00 ON 02 JUL 2005
L1 78 S RAR ANTAGONIST?
L2 2641 S RAR
L3 4870 S ATOPY

10676089

L4 21707 S PSORIASIS
L5 12 S L2 (P) L4
L6 0 S L2 (P) L3
L7 0 S L2 AND L3
L8 7800 S RETINOID
L9 3 S L8 AND ATOPY

=> d l5 1-12 bib abs kwic

L5 ANSWER 1 OF 12 MEDLINE on STN
AN 2000435655 MEDLINE
DN PubMed ID: 10329471
TI Identification of the AP1-antagonism domain of retinoic acid receptors.
AU DiSepio D; Sutter M; Johnson A T; Chandraratna R A; Nagpal S
CS Department of Biology, Allergan Inc., Irvine, California 92713, USA.
SO Molecular cell biology research communications : MCBRC, (1999 Apr) 1 (1) 7-13.
Journal code: 100889076. ISSN: 1522-4724.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
ED Entered STN: 20000928
Last Updated on STN: 20000928
Entered Medline: 20000921
AB Retinoids are therapeutically effective in the treatment of **psoriasis**, photoaging, acne, and certain cancers. Some of the therapeutic actions of retinoids can be ascribed to retinoic acid receptor (**RAR**)-mediated antagonism of AP1-dependent gene expression. The increased activity of transcription factor AP1, a complex of oncoproteins Jun and Fos, is associated with cell growth and proliferation. Retinoids, on the other hand, inhibit cell proliferation and affect differentiation, activities that possibly stem from an antagonism of AP1-mediated gene expression by RARs. To gain insight into the molecular mechanism of **RAR**-AP1 interaction, we have identified the regions of the **RAR** required for AP1 antagonism. We demonstrate that the AP1 antagonism domain of **RAR** is a complex of the core of the DNA binding domain and the hydrophobic zipper region. Further, both monomeric **RAR** and **RAR**-RXR heterodimers inhibit the expression of an AP1 reporter. CREB binding protein (CBP) has been described as a cofactor for AP1, various nuclear hormone receptor proteins including RARs, and certain other transcription factors and is required for their transactivation properties. Therefore, CBP has been proposed as a common limiting cofactor that can account for inhibition of AP1-dependent gene expression by RARs. Interestingly, however, our results along with previously reported observations suggest that in addition to CBP, there may be other limiting cofactor(s) responsible for mutual transrepression of **RAR** and AP1.
AB Retinoids are therapeutically effective in the treatment of **psoriasis**, photoaging, acne, and certain cancers. Some of the therapeutic actions of retinoids can be ascribed to retinoic acid receptor (**RAR**)-mediated antagonism of AP1-dependent gene expression. The increased activity of transcription factor AP1, a complex of oncoproteins Jun and Fos, is. . . that possibly stem from an antagonism of AP1-mediated gene expression by RARs. To gain insight into the molecular mechanism of **RAR**-AP1 interaction, we have identified the regions of the **RAR** required for AP1 antagonism. We demonstrate that the

AP1 antagonism domain of **RAR** is a complex of the core of the DNA binding domain and the hydrophobic zipper region. Further, both monomeric **RAR** and **RAR**-RXR heterodimers inhibit the expression of an AP1 reporter. CREB binding protein (CBP) has been described as a cofactor for AP1,. . . previously reported observations suggest that in addition to CBP, there may be other limiting cofactor(s) responsible for mutual transrepression of **RAR** and AP1.

L5 ANSWER 2 OF 12 MEDLINE on STN
AN 2000291536 MEDLINE
DN PubMed ID: 10828316
TI Recent developments in receptor-selective retinoids.
AU Nagpal S; Chandraratna R A
CS Retinoid Research, Department of Biology and Chemistry, Allergan Inc., Irvine, CA-92713, USA.
SO Current pharmaceutical design, (2000 Jun) 6 (9) 919-31. Ref: 71
Journal code: 9602487. ISSN: 1381-6128.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200007
ED Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000731
AB Natural (all trans-retinoic acid, RA) and synthetic retinoids exhibit potent anti-proliferative, normalization of differentiation and anti-inflammatory activities which appear to account for their therapeutic effects in acne, **psoriasis**, photoaging, precancerous lesions and established cancers. Although RA has shown considerable promise in dermatologic indications, certain side effects have restricted its use as a choice of agent for chronic administration. Systematic synthesis of receptor-selective retinoids has resulted in two topical drugs, Tazorac/Zorac (tazarotene) and Differin (adapalene). Tazorac is indicated for **psoriasis** and acne and Differin gel for the treatment of acne. These drugs bind to the retinoic acid receptor (**RAR**) family members. Various **RAR** subtype-specific and function-selective retinoids have been synthesized. These retinoids, which are in various stages of pre-clinical development for the treatment of cancers, **psoriasis** and as an antidote to Accutane-mediated mucocutaneous toxicity, will also be discussed in this review. Discovery of another retinoid receptor, retinoid X receptor (RXR), revealed that RXR-specific retinoids already existed in retinoid chemical libraries. Structure activity relationship studies based upon binding and transactivation assays led to the synthesis of RXR-specific ligands with high affinities for RXR subtypes. These compounds were found to be effective in the treatment of hyperglycemia in animal models of type II diabetes. The discovery of novel retinoids along with an increased understanding of the biological functions and mechanisms of action of retinoid receptors are likely to result in improved treatments for existing responsive indications and identification of new retinoid therapeutic targets.
AB . . . retinoids exhibit potent anti-proliferative, normalization of differentiation and anti-inflammatory activities which appear to account for their therapeutic effects in acne, **psoriasis**, photoaging, precancerous lesions and established cancers. Although RA has shown

considerable promise in dermatologic indications, certain side effects have restricted. . . Systematic synthesis of receptor-selective retinoids has resulted in two topical drugs, Tazorac/Zorac (tazarotene) and Differin (adapalene). Tazorac is indicated for **psoriasis** and acne and Differin gel for the treatment of acne. These drugs bind to the retinoic acid receptor (**RAR**) family members. Various **RAR** subtype-specific and function-selective retinoids have been synthesized. These retinoids, which are in various stages of pre-clinical development for the treatment of cancers, **psoriasis** and as an antidote to Accutane-mediated mucocutaneous toxicity, will also be discussed in this review. Discovery of another retinoid receptor,. . .

L5 ANSWER 3 OF 12 MEDLINE on STN
AN 2000105744 MEDLINE
DN PubMed ID: 10637371
TI Therapeutic applications for ligands of retinoid receptors.
AU Thacher S M; Vasudevan J; Chandraratna R A
CS Retinoid Research, Departments of Biology and Chemistry, Allergan Inc., Irvine, California 92623, USA.
SO Current pharmaceutical design, (2000 Jan) 6 (1) 25-58. Ref: 216
Journal code: 9602487. ISSN: 1381-6128.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200003
ED Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000315
AB Synthetic retinoids, ligands for the **RAR** and RXR members of the steroid/thyroid superfamily of nuclear hormone receptors, are used for the treatment of **psoriasis**, acne, photoaging and cancer. Retinoid mechanisms of action for these conditions largely involve effects on epithelial differentiation and modulation of inflammation with some impact on the immune system. Retinoid medicinal chemistry in recent years has identified ligands highly specific for one of the three **RAR** subtypes (**RAR**-alpha) and for the RXR family of receptors, as well as antagonists for the RARs, RARalpha and the RXRs. Structure-activity relationships among the novel retinoid classes are reviewed along with potential therapeutic activities and side effects. **RAR**-alpha specific retinoids inhibit cancer cell growth but lack other retinoid toxicities, including skin irritation now ascribed to **RAR**-gama. RXR-specific retinoids lower blood glucose in animal models of type 2 diabetes albeit with a potential for mild hypothyroidism. Function-selective retinoids, especially a class of **RAR** antagonists called inverse agonists, have unexpected gene regulatory activity. Given the diverse properties and tissue distributions of the retinoid receptors, synthesis of additional classes of receptor-specific and function-selective ligands has the potential to produce novel therapeutic applications.
AB Synthetic retinoids, ligands for the **RAR** and RXR members of the steroid/thyroid superfamily of nuclear hormone receptors, are used for the treatment of **psoriasis**, acne, photoaging and cancer. Retinoid mechanisms of action for these conditions largely involve effects on epithelial differentiation and modulation of. . . on the immune system. Retinoid medicinal chemistry in recent years has identified ligands highly

specific for one of the three **RAR** subtypes (**RAR**-alpha) and for the RXR family of receptors, as well as antagonists for the RARs, RARalpha and the RXRs. Structure-activity relationships among the novel retinoid classes are reviewed along with potential therapeutic activities and side effects. **RAR**-alpha specific retinoids inhibit cancer cell growth but lack other retinoid toxicities, including skin irritation now ascribed to **RAR**-gama. RXR-specific retinoids lower blood glucose in animal models of type 2 diabetes albeit with a potential for mild hypothyroidism. Function-selective retinoids, especially a class of **RAR** antagonists called inverse agonists, have unexpected gene regulatory activity. Given the diverse properties and tissue distributions of the retinoid receptors,. . .

L5 ANSWER 4 OF 12 MEDLINE on STN
AN 1999412298 MEDLINE
DN PubMed ID: 10459139
TI Retinoids and psoriasis: novel issues in retinoid pharmacology and implications for psoriasis treatment.
AU Saurat J H
CS Department of Dermatology University Hospital Geneva, Switzerland.
SO Journal of the American Academy of Dermatology, (1999 Sep) 41 (3 Pt 2) S2-6. Ref: 20
Journal code: 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990930
AB Oral synthetic retinoids have been established as effective systemic therapy for **psoriasis** since their introduction for clinical use in the 1970s. Acitretin, the free acid of etretinate and its active metabolite, has replaced etretinate as the retinoid of choice for treating **psoriasis** because of its more favorable pharmacokinetic profile. Despite the demonstrated clinical success of retinoid therapy in **psoriasis** and other proliferative skin disorders, their mechanism of action has not been fully elucidated. Altered vitamin A metabolism, characterized by an increase in the formation of retinoic acid, has been demonstrated in psoriatic lesions and is potentially influenced by cytokines such as interferon gamma, which is present in high levels in these lesions. Synthetic retinoids such as acitretin may interfere with such cytokine-induced alterations. Studies on nuclear retinoic acid receptors have shown that acitretin activates all 3 receptor subtypes (**RAR**-alpha, -beta, and -gamma) without measurable receptor binding; this paradox remains unexplained. Further studies on nuclear receptor binding and activity, including possible receptor crosstalk with vitamin D nuclear receptors, promise to enhance understanding of the usefulness of retinoids in treatment of **psoriasis.**
AB Oral synthetic retinoids have been established as effective systemic therapy for **psoriasis** since their introduction for clinical use in the 1970s. Acitretin, the free acid of etretinate and its active metabolite, has replaced etretinate as the retinoid of choice for treating **psoriasis** because of its more favorable pharmacokinetic profile. Despite the demonstrated clinical success of retinoid therapy in

psoriasis and other proliferative skin disorders, their mechanism of action has not been fully elucidated. Altered vitamin A metabolism, characterized by. . . interfere with such cytokine-induced alterations. Studies on nuclear retinoic acid receptors have shown that acitretin activates all 3 receptor subtypes (**RAR**-alpha, -beta, and -gamma) without measurable receptor binding; this paradox remains unexplained. Further studies on nuclear receptor binding and activity, including. . . possible receptor crosstalk with vitamin D nuclear receptors, promise to enhance understanding of the usefulness of retinoids in treatment of **psoriasis.**

L5 ANSWER 5 OF 12 MEDLINE on STN
AN 1998291169 MEDLINE
DN PubMed ID: 9627699
TI Vitamin D-retinoid association: molecular basis and clinical applications.
AU Carlberg C; Saurat J H
CS Clinique de Dermatologie, Hopital Cantonal Universitaire, Geneva, Switzerland.
SO journal of investigative dermatology. Symposium proceedings / the Society for Investigative Dermatology, Inc. [and] European Society for Dermatological Research, (1996 Apr) 1 (1) 82-6. Ref: 55
Journal code: 9609059. ISSN: 1087-0024.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625
AB The molecular structure of the biological active form of vitamin D, 1 alpha,25-dihydroxyvitamin D3 (VD), and the vitamin A derivatives all-trans and 9-cis retinoic acid (RA) are not related. The nuclear receptors for VD (VDR) and retinoids (**RAR** and RXR), however, are members of the same superfamily of ligand-activated transcription factors. We observed stable VDR-RXR and VDR-**RAR** heterodimers in solution and their transcriptional activity on different types of response elements. Both heterodimeric complexes are activated by VD, but, depending on the relative expression of the nuclear receptors, retinoids can have either co-stimulating or repressing effects. This demonstrates that VD and retinoid signaling are linked at the level of gene regulation and may explain the similar effects of both hormones on cell proliferation and differentiation. This concept may be applied for treating skin diseases, with the hope that a synergism will be observed, allowing better responses with lower doses of each compound. Preliminary observations suggest that **psoriasis**, cutaneous T-cell lymphomas, and actinic keratoses might be potential targets for VD-retinoid associations.
AB . . . vitamin A derivatives all-trans and 9-cis retinoic acid (RA) are not related. The nuclear receptors for VD (VDR) and retinoids (**RAR** and RXR), however, are members of the same superfamily of ligand-activated transcription factors. We observed stable VDR-RXR and VDR-**RAR** heterodimers in solution and their transcriptional activity on different types of response elements. Both heterodimeric complexes are activated by VD,. . . hope that a synergism will be observed, allowing better responses with lower doses of each compound. Preliminary observations suggest that **psoriasis**, cutaneous

T-cell lymphomas, and actinic keratoses might be potential targets for VD-retinoid associations.

L5 ANSWER 6 OF 12 MEDLINE on STN
AN 97416601 MEDLINE
DN PubMed ID: 9270551
TI Tazarotene: the first receptor-selective topical retinoid for the treatment of psoriasis.
CM Comment in: J Am Acad Dermatol. 1999 Dec;41(6):1049-50. PubMed ID: 10570404
AU Chandraratna R A
CS Allergan, Inc., Irvine CA 92713, USA.
SO Journal of the American Academy of Dermatology, (1997 Aug) 37 (2 Pt 3) S12-7. Ref: 34
Journal code: 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970926
Last Updated on STN: 20000209
Entered Medline: 19970915
AB Tazarotene belongs to a novel, nonisomerizable class of retinoic acid receptor (**RAR**)-specific retinoids, the acetylenic retinoids, and is the first topical retinoid developed for the treatment of **psoriasis.** Tazarotene targets the keratinocyte and modulates the major causes of **psoriasis.** Tazarotene is rapidly metabolized by esterase to the active free acid tazarotenic acid, which is rapidly eliminated in animal species. Tazarotene selectively transactivates **RAR** beta and **RAR** gamma subtypes and is inactive at retinoid X receptors (RXRs). This receptor selectivity could contribute to an optimized therapeutic index. Tazarotene has low systemic absorption after topical administration. In preclinical toxicity studies, high topical doses produced reversible topical irritation, and lower doses were well tolerated. Topical doses were neither teratogenic nor carcinogenic and were not sensitizing, phototoxic, or photosensitizing. The topical delivery of tazarotene and limited systemic exposure apparently result in a very low potential for systemic effects.
AB Tazarotene belongs to a novel, nonisomerizable class of retinoic acid receptor (**RAR**)-specific retinoids, the acetylenic retinoids, and is the first topical retinoid developed for the treatment of **psoriasis.** Tazarotene targets the keratinocyte and modulates the major causes of **psoriasis.** Tazarotene is rapidly metabolized by esterase to the active free acid tazarotenic acid, which is rapidly eliminated in animal species. Tazarotene selectively transactivates **RAR** beta and **RAR** gamma subtypes and is inactive at retinoid X receptors (RXRs). This receptor selectivity could contribute to an optimized therapeutic index.. . .

L5 ANSWER 7 OF 12 MEDLINE on STN
AN 97297774 MEDLINE
DN PubMed ID: 9153406
TI The isolation and characterization of purified heterocomplexes of recombinant retinoic acid receptor and retinoid X receptor ligand binding domains.

10676089

AU Tian K; Norris A W; Lin C L; Li E
CS Department of Medicine, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
NC 5-T32GM07200 (NIGMS)
DK40172 (NIDDK)
DK49684 (NIDDK)
SO Biochemistry, (1997 May 13) 36 (19) 5669-76.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
ED Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970609
AB Retinoic acid exerts many of its biological effects by interaction with heterocomplexes of nuclear retinoic acid receptors (RARs) and retinoid X receptors (RXRs). To further examine this interaction, a glutathione S-transferase (GST) fusion protein containing the ligand binding domain of human RXR alpha has been used to copurify the ligand binding domain of human **RAR** gamma by affinity chromatography over glutathione-agarose. Complexes of recombinant **RAR**-RXR ligand binding domains retaining full ligand binding capacity were purified, and their interactions with various retinoids were characterized by fluorometric titration and photoaffinity labeling. Analyses of the distribution of limiting amounts of [3H]-all-trans-retinoic acid between cytoplasmic retinoic acid binding proteins, CRABP-I and CRABP-II, and the purified heterocomplexes indicate that all-trans-retinoic acid binds with comparable affinity to CRABP-I and the heterocomplexes, but with approximately 10-fold less affinity to CRABP-II. The aromatic retinoid acitretin, which is used in the treatment of **psoriasis**, binds relatively poorly to the purified heterocomplexes, although it binds with high affinity to the CRABPs. Acitretin displaces [3H]-all-trans-retinoic acid from the CRABPs and increases retinoic acid occupancy of the heterocomplexes. These results suggest that certain retinoids could potentially perturb the distribution of endogenous retinoic acid between the CRABPs and the nuclear receptors and thus affect retinoid signaling. The purified recombinant complexes should provide a useful model system for further structural analysis of the dimerization interface between the **RAR** and RXR ligand binding domains.
AB . . . containing the ligand binding domain of human RXR alpha has been used to copurify the ligand binding domain of human **RAR** gamma by affinity chromatography over glutathione-agarose. Complexes of recombinant **RAR**-RXR ligand binding domains retaining full ligand binding capacity were purified, and their interactions with various retinoids were characterized by fluorometric. . . heterocomplexes, but with approximately 10-fold less affinity to CRABP-II. The aromatic retinoid acitretin, which is used in the treatment of **psoriasis**, binds relatively poorly to the purified heterocomplexes, although it binds with high affinity to the CRABPs. Acitretin displaces [3H]-all-trans-retinoic acid. . . The purified recombinant complexes should provide a useful model system for further structural analysis of the dimerization interface between the **RAR** and RXR ligand binding domains.

L5 ANSWER 8 OF 12 MEDLINE on STN
AN 97228814 MEDLINE

10676089

DN PubMed ID: 9074840
TI Current use and future potential role of retinoids in dermatology.
AU Orfanos C E; Zouboulis C C; Almond-Roesler B; Geilen C C
CS Department of Dermatology, University Medical Center Benjamin Franklin, Free University of Berlin, Germany.
SO Drugs, (1997 Mar) 53 (3) 358-88. Ref: 262
Journal code: 7600076. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970609
Last Updated on STN: 19970609
Entered Medline: 19970528
AB Since their introduction 15 years ago, retinoids have been increasingly used for topical and systemic treatment of **psoriasis** and other hyperkeratotic and parakeratotic skin disorders, keratotic genodermatoses, severe acne and acne-related dermatoses, and also for therapy and/or chemoprevention of skin cancer and other neoplasia. Oxidative metabolites of vitamin A (retinol) are natural retinoids present at low levels in the peripheral blood. Synthetic retinoids are classified into 3 generations including nonaromatic, monoaromatic and polyaromatic compounds. They are detectable in plasma 30-60 minutes after systemic administration, and reach maximum concentrations 2 to 4 hours later. Elimination half-life is 10 to 20 hours for isotretinoin, 80 to 175 days for etretinate and 2 to 4 days for, trans-acitretin; the latter, however, partially converts into etretinate. Retinoid concentrations in skin are rather low in contrast to subcutaneous fat tissue. Intracellularly, retinoids interact with cytosolic proteins and specific nuclear receptors. Two classes of nuclear receptors have been suggested to mediate retinoid activity at the molecular level, RARs and RXRs. The expression of retinoid receptors is tissue specific; skin mainly espresses **RAR** gamma and RXR alpha. Retinoids affect epidermal cell growth and differentiation as well as sebaceous gland activity and exhibit immunomodulatory and anti-inflammatory properties. Current retinoid research targets the development of receptor-selective retinoids for tailoring and/or improving their therapeutic profile. Currently, tretinoin is used systemically for acute promyelocytic leukaemia, etretinate and acitretin for **psoriasis** and related disorders, as well as other disorders of keratinisation and isotretinoin for seborrhoea, severe acne, rosacea and acneiform dermatoses. Systemic retinoids are also applied for chemoprevention of epithelial skin cancer and cutaneous T cell lymphoma. The major adverse effect of retinoids is teratogenicity; all other adverse effects are dose-dependent and controllable. Contraception is, therefore, essential during retinoid treatment in women of child-bearing age. Clinical monitoring requires physical examination for adverse effects every 3 to 4 weeks and proper laboratory investigations, also including analysis of retinoid bioavailability in selected cases. Topical retinoids are rapidly developing at present and seem promising for the future; their clinical application includes acne, aging, photodamage, precanceroses, skin cancer and disorders of skin pigmentation. The development of receptor-specific retinoids for topical treatment of **psoriasis** and/or acne may lead to interesting new compounds based on our current concepts of retinoid function.
AB Since their introduction 15 years ago, retinoids have been increasingly

used for topical and systemic treatment of **psoriasis** and other hyperkeratotic and parakeratotic skin disorders, keratotic genodermatoses, severe acne and acne-related dermatoses, and also for therapy and/or chemoprevention. . . retinoid activity at the molecular level, RARs and RXRs. The expression of retinoid receptors is tissue specific; skin mainly espresses **RAR** gamma and RXR alpha. Retinoids affect epidermal cell growth and differentiation as well as sebaceous gland activity and exhibit immunomodulatory. . . for tailoring and/or improving their therapeutic profile. Currently, tretinoin is used systemically for acute promyelocytic leukaemia, etretinate and acitretin for **psoriasis** and related disorders, as well as other disorders of keratinisation and isotretinoin for seborrhoea, severe acne, rosacea and acneiform dermatoses.. . . acne, aging, photodamage, precanceroses, skin cancer and disorders of skin pigmentation. The development of receptor-specific retinoids for topical treatment of **psoriasis** and/or acne may lead to interesting new compounds based on our current concepts of retinoid function.

L5 ANSWER 9 OF 12 MEDLINE on STN
AN 97118505 MEDLINE
DN PubMed ID: 8959347
TI Negative regulation of two hyperproliferative keratinocyte differentiation markers by a retinoic acid receptor-specific retinoid: insight into the mechanism of retinoid action in psoriasis.
AU Nagpal S; Thacher S M; Patel S; Friant S; Malhotra M; Shafer J; Krasinski G; Asano A T; Teng M; Duvic M; Chandraratna R A
CS Department of Biology, Allergan Inc., Irvine, California 92713, USA.
NC R01AR39915 (NIAMS)
SO Cell growth & differentiation : molecular biology journal of the American Association for Cancer Research, (1996 Dec) 7 (12) 1783-91.
Journal code: 9100024. ISSN: 1044-9523.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970307
AB Retinoids down-regulate the expression of metalloproteinases, cytokines, and other genes involved in cell proliferation and inflammation. Tazarotene (AGN 190168), a retinoic acid receptor (**RAR**)-specific retinoid, is effective in the treatment of **psoriasis**, a hyperproliferative and inflammatory skin disease. Because negative regulation of genes appears to be important in the antiproliferative and antiinflammatory action of retinoids, we studied the down-regulation of genes in skin raft cultures by this antipsoriatic retinoid. By subtraction hybridization, we found that migration inhibitory factor-related protein (MRP-8) and skin-derived anti-leukoproteinase (SKALP) are down-regulated by AGN 190168. MRP-8 and SKALP are overexpressed in psoriatic lesions as compared to the normal epidermis, and they are markers of hyperproliferative keratinocyte differentiation. We also show that MRP-8 expression is retinoid inhibitable in cultured keratinocytes induced to differentiate with 10% serum or IFN-gamma, and that MRP-8 is inhibited by **RAR** but not by retinoid X receptor-specific retinoids in a dose-dependent manner. Finally, MRP-8, SKALP, and the previously characterized differentiation marker, transglutaminase I, are all down-regulated in vivo in psoriatic lesions

after treatment with AGN 190168 in comparison to placebo. Taken together, these data suggest that these markers may be down-regulated by tazarotene in **psoriasis** through direct action on keratinocyte gene expression rather than by an overall tazarotene effect on lesional therapeutic status.

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L5 ANSWER 10 OF 12 MEDLINE on STN
AN 97105538 MEDLINE
DN PubMed ID: 9035701
TI Tazarotene--first of a new generation of receptor-selective retinoids.
AU Chandraratna R A
CS Retinoid Research, Allergan Inc., Irvine, CA 92713-9534, USA.
SO British journal of dermatology, (1996 Oct) 135 Suppl 49 18-25.
Journal code: 0004041. ISSN: 0007-0963.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
ED Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970227

AB Tazarotene is a topically applied retinoid that targets the skin, the site of the fundamental defect(s) in **psoriasis**, modulating the major causes of the disease and achieving sustained efficacy. In vitro, binding of tazarotenic acid has been demonstrated to retinoic acid receptors (RARs), the probable molecular target of retinoid action in adult human skin, but not to retinoid X receptors (RXRs). In gene activation assays, tazarotene is selective for the **RAR** beta and **RAR** gamma subtypes. This selectivity could theoretically limit undesirable effects at the receptor level. In vitro, animal and clinical evidence reveals that topical tazarotene modulates all three pathogenic factors in **psoriasis**: abnormal keratinocyte differentiation, hyperproliferation, and increased expression of inflammatory markers. Tazarotene is minimally absorbed systemically after topical administration. Tazarotene is rapidly metabolized by esterase metabolism to its active free-acid form, tazarotenic acid, which has a relatively short elimination half-life (1-2 h). The pharmacokinetic profile of tazarotenic acid is predictable, with no significant accumulation. In preclinical toxicity studies, high topical doses produced only reversible topical irritation, and lower doses were well tolerated. Topical doses were neither carcinogenic nor teratogenic, had no effect on fertility or general reproduction, and were not phototoxic, sensitizing, or

photoallergenic. The pharmacological selectivity of tazarotene and limited systemic exposure result in minimal systemic effects, while the lesser cytotoxic effects (relative to other retinoids) result in reduced local effects.

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L5 ANSWER 11 OF 12 MEDLINE on STN
AN 96007653 MEDLINE
DN PubMed ID: 7547381
TI In situ detection of retinoid-X receptor expression in normal and psoriatic human skin.
AU Reichrath J; Munssinger T; Kerber A; Rochette-Egly C; Chambon P; Bahmer F A; Baum H P
CS Department of Dermatology, Universitat des Saarlandes, Homburg, Germany.
SO British journal of dermatology, (1995 Aug) 133 (2) 168-75.
Journal code: 0004041. ISSN: 0007-0963.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199510
ED Entered STN: 19951227
Last Updated on STN: 19951227
Entered Medline: 19951030

AB Increasing evidence suggests that the retinoid-X receptors RXR(-alpha,-beta,-gamma) play a crucial part in regulating the transcriptional activity of several steroid hormone receptors, including 1,25-dihydroxyvitamin D3 receptors (VDR) and retinoic acid receptors (**RAR**-alpha,-beta,-gamma). We developed a new technique for immunohistochemical in situ detection of RXR receptors, and investigated the localization of RXR-alpha in normal and psoriatic human skin using a recently raised corresponding specific antibody. RXR-alpha positive cells related to the skin were phenotyped by sequential sections and a double-labelling procedure for the simultaneous demonstration of this nuclear receptor and cell membrane antigens, as well as cytokeratin 10, HLA-DR and vimentin. Our findings indicate that: (i) RXR-alpha is strongly expressed in normal and psoriatic human skin; (ii) most of the cell types in normal human skin, including keratinocytes, melanocytes, fibroblasts and skin immune cells such as Langerhans cells, reveal strong nuclear immunoreactivity for RXR-alpha, with less cytoplasmic staining; (iii) altered levels or distribution of RXR-alpha in the skin do not appear to be involved in the genesis of **psoriasis** vulgaris, but subepidermal and subcellular distribution suggest a function of RXR-alpha in the transition from proliferation to differentiation in epidermal keratinocytes; (iv) expression in the hair follicle points to a contribution from RXR-alpha to hair growth.

AB . . . part in regulating the transcriptional activity of several steroid hormone receptors, including 1,25-dihydroxyvitamin D3 receptors (VDR) and retinoic acid receptors (**RAR**-alpha,-beta,-gamma). We developed a new technique for immunohistochemical in situ detection of RXR receptors, and investigated the localization of RXR-alpha in. . . (iii) altered levels or distribution of RXR-alpha in the skin do not appear to be involved in the genesis of **psoriasis** vulgaris, but subepidermal and subcellular distribution suggest a function of RXR-alpha in the transition from proliferation to differentiation in epidermal. . .

L5 ANSWER 12 OF 12 MEDLINE on STN
AN 95122546 MEDLINE
DN PubMed ID: 7822331
TI Separation of transactivation and AP1 antagonism functions of retinoic acid receptor alpha.
AU Nagpal S; Athanikar J; Chandraratna R A
CS Department of Biology, Allergan Inc., Irvine, California 92713.
SO Journal of biological chemistry, (1995 Jan 13) 270 (2) 923-7.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502
ED Entered STN: 19950223
Last Updated on STN: 19970203
Entered Medline: 19950213
AB Retinoic acid receptors (RARs) regulate gene expression either by directly binding to the **RAR**-responsive elements or by antagonizing the action of c-Jun/c-Fos (AP1). AP1 is involved in the expression of metalloproteases, cytokines and other factors which play critical roles in the turnover of extracellular matrix, inflammation and hyperproliferation in diseases such as **psoriasis**, rheumatoid arthritis and in tumor metastases. We demonstrate here that synthetic retinoids inhibit 12-O-tetradecanoylphorbol-14-acetate-induced transcription from the stromelysin AP1 motif through **RAR** alpha, -beta, and -gamma. Interestingly, these diaryl acetylenic retinoids, which are potent agonists only for **RAR** beta and **RAR** gamma, but not for **RAR** alpha, in transactivation assays, are able to inhibit AP1-dependent gene expression through **RAR** alpha. Thus these analogs can differentially affect the transactivation and AP1 antagonistic functions of **RAR** alpha. These results demonstrate that the transactivation and AP1 antagonistic functions are separable, and it should be possible to develop retinoids that are completely specific for AP1 antagonism through all RARs. Furthermore, using an **RAR** -selective ligand, we also demonstrate the separation of ligand binding and AP1 antagonism functions of RARs.
AB Retinoic acid receptors (RARs) regulate gene expression either by directly binding to the **RAR**-responsive elements or by antagonizing the action of c-Jun/c-Fos (AP1). AP1 is involved in the expression of metalloproteases, cytokines and other factors which play critical roles in the turnover of extracellular matrix, inflammation and hyperproliferation in diseases such as **psoriasis**, rheumatoid arthritis and in tumor metastases. We demonstrate here that synthetic retinoids inhibit 12-O-tetradecanoylphorbol-14-acetate-induced transcription from the stromelysin AP1 motif through **RAR** alpha, -beta, and -gamma. Interestingly, these diaryl acetylenic retinoids, which are potent

agonists only for **RAR** beta and **RAR** gamma, but not for **RAR** alpha, in transactivation assays, are able to inhibit AP1-dependent gene expression through **RAR** alpha. Thus these analogs can differentially affect the transactivation and AP1 antagonistic functions of **RAR** alpha. These results demonstrate that the transactivation and AP1 antagonistic functions are separable, and it should be possible to develop retinoids that are completely specific for AP1 antagonism through all RARs. Furthermore, using an **RAR** -selective ligand, we also demonstrate the separation of ligand binding and AP1 antagonism functions of RARs.

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L10 ANSWER 1 OF 7 MEDLINE on STN
AN 2004433630 MEDLINE
DN PubMed ID: 15339073
TI Chronic idiopathic and chronic autoimmune urticaria: clinical and immunopathological features of 68 subjects.
AU Caproni Marzia; Volpi Walter; Giomi Barbara; Cardinali Carla; Antiga Emiliano; Melani Lucilla; Dagata Alberino; Fabbri Paolo
CS Department of Dermatological Sciences, II Dermatological Clinic, University of Florence, Florence, Italy.. marziacaproni@virgilio.it
SO Acta dermato-venereologica, (2004) 84 (4) 288-90.
Journal code: 0370310. ISSN: 0001-5555.
CY Norway
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200411
ED Entered STN: 20040902
Last Updated on STN: 20041219
Entered Medline: 20041130
AB Skin tests with autologous serum elicit an immediate wheal-and-flare response in about 30-50% of chronic idiopathic urticaria subjects, suggesting that an autoimmune mechanism might be involved in the pathogenesis of this disease. The aim of the present work, involving 68 subjects with chronic idiopathic urticaria, was to distinguish between the serum-positive and serum-negative cases and highlight the clinical differences between the two groups on the basis of the Breneman scale score. We also tried to correlate the finding of a positive response to the autologous serum skin test with other autoimmune diatheses or fully developed autoimmune disorders. Our results did not demonstrate any significant differences between the two groups with regard to mean age, sex distribution, angioedema and mucosal/**cutaneous atopy** . However, all subjects with positive autologous serum skin test presented more severe clinical features than serum-negative subjects. We found no differences between the two groups in the incidence of autoimmune disease.

L10 ANSWER 2 OF 7 MEDLINE on STN
AN 1999397185 MEDLINE
DN PubMed ID: 10467854
TI [Skin diseases related to work: how to approach them?].
Maladies cutanees liees au travail: comment les aborder?.
AU Perrenoud D
CS Service de dermatologie (DHURDV), CHUV, Lausanne.
SO Revue medicale de la Suisse romande, (1999 Jul) 119 (7) 593-8. Ref: 9
Journal code: 0421524. ISSN: 0035-3655.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 199909
ED Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990924
AB Work-related skin problems are frequent and mainly affect the hands. They

can be approached by looking for indications of the 3 principal underlying types of dermatitis: irritant, allergic, or chronic. Irritation and contact allergy are closely associated: the irritation facilitates the flowering of the allergy. Skin irritation due to working conditions is often multi-causal and repetitive. **Cutaneous atopy** --but not that which is only respiratory or mucosal--is the main genetic risk factor for the development of a work-related skin disease. The characteristics of irritation and allergy tend to merge when the lesions become chronic. An 8-step process is suggested to establish the causal relationship between potentially damaging substances in the workplace and the resulting skin problems. In Switzerland, professional dermatitis falls under the purview of the accident insurance laws. These laws recognize causal responsibility whenever the work substances or activities are preponderant over non-professional causes.

L10 ANSWER 3 OF 7 MEDLINE on STN
AN 1999191577 MEDLINE
DN PubMed ID: 10091477
TI Recent studies of cutaneous nociception in atopic and non-atopic subjects.
AU Heyer G R; Hornstein O P
CS Department of Dermatology, University of Erlangen-Nuernberg, Germany.
SO Journal of dermatology, (1999 Feb) 26 (2) 77-86. Ref: 43
Journal code: 7600545. ISSN: 0385-2407.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990517
Last Updated on STN: 19990517
Entered Medline: 19990430
AB Itching reflects a distinct quality of cutaneous nociception elicited by chemical or other stimuli to neuronal receptors at the superficial layers of the skin and muco-cutaneous orifices. Although recent experimental studies of the conduction and perception of itch have yielded deeper insight into the physiology of this sensory quality, little is known about the neuromechanisms involved in pruritus accompanying many inflammatory skin diseases, in particular, in atopic eczema. Previous case-control studies of our research group with patients suffering from atopic eczema (AE) revealed significantly diminished itch perception after iontophoretic application of different doses of histamine as well as substance P (i.c. injected). Further experiments using acetylcholine (ACh, i.c.) clearly demonstrated that ACh elicits pruritus instead of pain in patients with AE. The first part of the present review deals with the results of our most recent case-control studies on histamine-induced itch perception in atopics devoid of eczema as well as in patients with urticaria or psoriasis compared to atopics with or without manifest eczema. We demonstrated that both focal itch and perifocal alloknesis (i.e., itch elicited by a slight mechanical, otherwise non-itching stimulus) were significantly reduced in eczema-free atopics yet were normal in non-atopics suffering from urticaria or psoriasis. In further studies using ACh i.c. injected into the uninvolved skin of patients with AE, lichen ruber, psoriasis, type IV contact eczema, or non-specific nummular eczema (n = 10/each group), all the atopics and 6/10 psoriatics felt itch instead of burning pain, but none of the others did. Different doses of vasoactive intestinal peptide (VIP) i.c. applied to the controls and the atopics with or without eczema did not markedly increase the intensity of

nociceptive sensations. However, ACh induced pain in the controls, pure pruritus in the atopics with acute eczema, and a 'mixture' of pain and itch in the atopics just free from eczema. Obviously, the quality of sensations evoked by ACh and VIP depends on the inflammatory or non-inflammatory state of the atopic skin. In a placebo-controlled, double blind study on histamine-induced focal itch and alloknesis with healthy subjects (n = 15) using naltrexone (opioid receptor antagonist) and cetirizine (H1-blocking agent), naltrexone was found to significantly reduce both itching and alloknesis. Cetirizine reduced focal itch but failed to influence the alloknesis phenomenon. The wheal and flare reaction was suppressed only by cetirizine. These different effects point to a mainly CNS-based activity of naltrexone but a peripheral level effect of cetirizine. Due to long-lasting experience with group sport as a supporting adjuvant for inpatients with AE, we evaluated, by clinical, psychometric, and physiological studies, the therapeutic efficacy of controlled physical exercise in addition to otherwise equal anti-eczematous therapy for both voluntary participants and non-participants in sports by performing several case-control studies, one followed-up to 6 months after the patients' discharge from the hospital. Regular moderate exercises neither deteriorated nor impeded the recovery from AE, ameliorated the participants' scratch controlling ability and significantly their depressed emotional mood. The non-participants failed to achieve these aims. Sweating-induced itch was inhibited in almost all participants if simple skin care (clearing by warm shower, ointment) and short-term rest were used by informed patients. In conclusion, there are several indications that itching is elicited in individuals inclined to **cutaneous atopy**, regardless of their eczematous or just eczema-free state, by a different physiological pathway from that in non-atopic individuals. Therefore, antipruritic agents influencing the centrally altered nociception of atopics are needed and may be expected in near future. (ABSTRACT TRUNCATED)

L10 ANSWER 4 OF 7 MEDLINE on STN
AN 97468660 MEDLINE
DN PubMed ID: 9327725
TI Feline atopic dermatitis. A model for Langerhans cell participation in disease pathogenesis.
AU Roosje P J; Whitaker-Menezes D; Goldschmidt M H; Moore P F; Willemse T; Murphy G F
CS Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, USA.
SO American journal of pathology, (1997 Oct) 151 (4) 927-32.
Journal code: 0370502. ISSN: 0002-9440.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199710
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971030
AB Atopic dermatitis is a disorder characterized by cutaneous exanthemata as a consequence of exaggerated eczematous reactions to topical and systemic allergens. Langerhans cells, expressing CD1a and HLA-DR, and dermal dendritic cells, expressing HLA-DR, are known to be potent antigen-presenting cells and are thought to play an important role in the pathogenesis of atopic dermatitis. The immunophenotype of lesional skin in atopic dermatitis in humans involves increased numbers of CD1a+/MHC

class II+ dendritic cells in addition to activated T cells, mast cells, and macrophages. To establish feline skin as a model for the study of human atopic dermatitis, and to elucidate the role of dendritic cells in feline atopic dermatitis, we investigated the presence of CD1a+ cells and MHC class II+ cells in the epidermis and dermis of lesional feline skin and in skin of healthy control animals. Immunohistochemistry revealed that MHC class II+ epidermal dendritic cells were CD1a+ in normal feline skin and significantly increased numbers of CD1a+ cells and MHC class II+ cells were present in the epidermis and dermis of lesional skin. These data provide the first correlative documentation of CD1a expression by feline dendritic cells containing Birbeck granules, and indicate the utility of feline skin in the study of human **cutaneous atopy.**

L10 ANSWER 5 OF 7 MEDLINE on STN
AN 94160540 MEDLINE
DN PubMed ID: 7509540
TI Canine cutaneous mast cells dispersion and histamine secretory characterization.
AU de Mora F; Garcia G; Ferrer L; Arboix M
CS Pharmacology Division, Veterinary Faculty, Autonomous University of Barcelona, Spain.
SO Veterinary immunology and immunopathology, (1993 Dec) 39 (4) 421-9. Journal code: 8002006. ISSN: 0165-2427.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
ED Entered STN: 19940406
Last Updated on STN: 19960129
Entered Medline: 19940328
AB In view of the high incidence of canine cutaneous atopic disease and the relevance of mast cells to its pathogenesis, it was considered important to isolate firstly cutaneous mast cells from normal dog skin and to assess the histamine secretory activity, as this can be further used as a tool for the study of canine skin mast cell pharmacology in **cutaneous atopy.** The procedure for canine dermal mast cell dispersion following a skin enzymatic digestion (as for previous human skin mast cell dispersion methods) is described in detail. The number of canine cutaneous mast cells yielded per gram of skin was 2.31 +/- 0.21 x 10(5) representing 1.00% of the total cutaneous cells. The total histamine content per mast cell is 4.93 +/- 0.39 pg. Net histamine release owing to stimulation by calcium ionophore A23187 (1 microM) and concanavalin A (1 mg ml-1) was respectively 32.17 +/- 3.56% and 20.39 +/- 2.41% of the total amount per cell. Viability and reactivity to both stimuli of dispersed cutaneous mast cells were similar to the results found in humans. The present study allows further research on the role of mast cells immunopharmacology in allergy by investigation of cells isolated from canine skin in naturally occurring or experimentally induced atopy in the dog to be undertaken.

L10 ANSWER 6 OF 7 MEDLINE on STN
AN 89069768 MEDLINE
DN PubMed ID: 3059093
TI [The concept of cryptic **cutaneous atopy** in contact reactions. Considerations on the clinical control over the subgroup of patients with frustrated **cutaneous atopy**].

10676089

El concepto de criptoatopia cutanea en las reacciones de contacto. Consideraciones de orden clinico sobre el subgrupo de la atopia cutanea frustre.

AU Grimalt F; Romaguera C; Lecha M; Mascaro J M

CS Departamento de Dermatologia Medico-Quirurgica y Venereologia de la Universidad de Barcelona.

SO Medicina cutanea ibero-latino-americana, (1988) 16 (3) 225-30. Journal code: 7601805. ISSN: 0210-5187.

CY Portugal

DT Journal; Article; (JOURNAL ARTICLE)

LA Spanish

FS Priority Journals

EM 198901

ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890123

AB Contact dermatitis, allergic or irritative, is not distributed by chance among the general population, but appears in a determined group of patients. The clinical and anamnestic picture of this group of patients (and that of their close blood relatives) is described. Clinical facts lead us to consider that group of patients as a subgroup of **cutaneous atopy.** The medical-legal importance which the acceptance of this type of patient could have on occupational contact dermatitis is pointed out. In contact dermatitis the factors of the person suffering the contact rather than those of the contact agents seem to be of decisive power in the response, although at the present moment, the possibility of carrying out analytical studies on the allergens and irritants is easier than on the patients who react to them.

L10 ANSWER 7 OF 7 MEDLINE on STN

AN 73052633 MEDLINE

DN PubMed ID: 4638088

TI [**Cutaneous atopy**].
Reflexions sur l'atopie cutanee.

AU Temime M P

SO Journal de medecine de Lyon, (1972 Sep 5) 53 (232) 1176-80. Journal code: 2985084R. ISSN: 0021-7883.

CY France

DT Journal; Article; (JOURNAL ARTICLE)

LA French

FS Priority Journals

EM 197302

ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19730202

10676089

L16 ANSWER 1 OF 1 MEDLINE on STN
AN 86224744 MEDLINE
DN PubMed ID: 3519696
TI Cyclosporin A.
CM Erratum in: J Am Acad Dermatol 1987 Jan;16(1 Pt 1):88
AU Page E H; Wexler D M; Guenther L C
SO Journal of the American Academy of Dermatology, (1986 May) 14 (5 Pt 1) 785-91. Ref: 76
Journal code: 7907132. ISSN: 0190-9622.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198606
ED Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860627
AB Cyclosporin A is a new immunosuppressive agent that selectively affects T helper cells without suppressing the bone marrow. Cyclosporin A has been used primarily to prevent rejection in organ transplantation and acute graft-versus-host disease. Studies suggest that it may be of benefit in **psoriasis**, pemphigus vulgaris, bullous pemphigoid, Behcet's disease, and collagen vascular disorders. Since cyclosporin A has a potentially important use in dermatology, and since a number of dermatologic side effects are seen as a consequence of its use, it is important that dermatologists be familiar with this drug.
AB . . . primarily to prevent rejection in organ transplantation and acute graft-versus-host disease. Studies suggest that it may be of benefit in **psoriasis**, pemphigus vulgaris, bullous pemphigoid, Behcet's disease, and collagen vascular disorders. Since cyclosporin A has a potentially important use in dermatology,. . .
CT . . . drug therapy
Collagen Diseases: DT, drug therapy
Cyclosporins: AE, adverse effects
*Cyclosporins: TU, therapeutic use
Gastrointestinal Diseases: CI, chemically induced
Gingival Hypertrophy: CI, chemically induced
Graft Rejection: DE, drug effects
Humans
Immunosuppression: AE, adverse effects
Kidney Diseases: CI, chemically induced
. . . Mycosis Fungoides: DT, drug therapy
Nervous System Diseases: CI, chemically induced
Pemphigoid, Bullous: DT, drug therapy
Pemphigus: DT, drug therapy
Psoriasis: DT, drug therapy
Sezary Syndrome: DT, drug therapy
*Skin Diseases: DT, drug therapy
Uveitis: DT, drug therapy